RN 396718-71-1 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-[(10-aminodecyl)amino]-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 396718-75-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)-1[6-[[2-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]ethyl]amino]-9H-purin-9yl]- (9CI) (CA INDEX NAME)

PAGE 2-A

RN 396718-77-7 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)-1-[6-[[4-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]butyl]amino]-9H-purin-9-yl]- (9CI) (CA INDEX NAME)

RN 396718-79-9 HCAPLUS

CN .beta.-D-Ribofuranuronamide, l-deoxy-N-ethyl-2,3-O-(l-methylethylidene)-l-[6-[[6-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]hexyl]amino]-9H-purin-9-yl]- (9CI) (CA INDEX NAME)

RN 396718-81-3 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)-1[6-[[8-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]octyl]amino]-9H-purin-9yl]- (9CI) (CA INDEX NAME)

PAGE 2-A | NO<sub>2</sub>

RN 396718-83-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-2,3-0-(1-methylethylidene)-1[6-[[10-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]decyl]amino]-9H-purin-9yl]- (9CI) (CA INDEX NAME)

PAGE 2-A

NO<sub>2</sub>

REFERENCE COUNT:

THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 40 OF 63 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1989:193332 HCAPLUS

DOCUMENT NUMBER:

TITLE:

110:193332

Preparation of adenosine-5'-carboxamide derivatives as

adenosine-2 receptor agonists, antipsychotics, and antihypertensives and pharmaceutical compositions

containing them

INVENTOR(S):

Hutchison, Alan J.

PATENT ASSIGNEE(S):

Ciba-Geigy A.-G., Switz.

SOURCE:

Eur. Pat. Appl., 17 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

13

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
EP 277917	A2	19880810	EP 1988-810050	19880129		
EP 277917	<b>A3</b>	19900328				

```
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE
     FI 8800405
                              19880805
                        Α
                                             FI 1988-405
                                                               19880129
     JP 63201196
                        A2
                              19880819
                                             JP 1988-21410
                                                               19880202
     DD 284679
                              19901121
                                             DD 1988-312611
                                                               19880202
                        A5
     DK 8800544
                              19880805
                                             DK 1988-544
                                                               19880203
                        Α
     NO 8800469
                              19880805
                                             NO 1988-469
                                                               19880203
                        Α
     AU 8811233
                        A1
                             19880818
                                             AU 1988-11233
                                                               19880203
     HU 46334
                        A2
                             19881028
                                             HU 1988-509
                                                               19880203
     HU 199155
                        В
                             19900129
     ZA 8800755
                        Α
                             19891025
                                             ZA 1988-755
                                                               19880203
PRIORITY APPLN. INFO .:
                                          US 1987-11169
                                                               19870204
OTHER SOURCE(S):
                          MARPAT 110:193332
```

AB The title compds. [I; R2 = H, alkyl, aralkyl; R3 = H, OH; R5 = NRR1 where R = H, alkyl and R1 = cycloalkyl, cycloalkylalkyl, 2-norbornanyl, etc.; R6 = R4NHCO where R4 = H, alkyl, aralkyl, cycloalkyl, hydroxyalkyl] (II) and their pharmaceutically acceptable salts, useful as adenosine-2 receptor agonists, antipsychotics, antithrombotics, and antihypertensives, are prepd. A mixt. of 2-chloro-2',3'-O-isopropylideneadenosine-5'-Nethylcarboxamide and 2-phenethylamine was heated at 130.degree. for 2 h to give 2-(2-phenethylamino)-2',3'-0-isopropylideneadenosine-5'-Nethylcarboxamide, which was heated with 1N HCl at 65.degree. for 1 h to give 2-(2-phenethylamino)-5'-N-ethylcarboxamide (III). In vivo studies of the adenosine-2 receptor agonistic activity of II using spontaneously hypertensive rats showed that II effectively lowered the blood pressure without any significant effect on the heart rate. One thousand tablets were prepd. from III 100.00, lactose 2400.00, corn starch 125.00, polyethyleneglycol 6000 150.00, Mg stearate 40.00 g, and water q.s. IT 120225-76-5P 120225-77-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of, in prepn. of adenosinecarboxamide derivs. as CNS and cardiovascular agents)

RN 120225-76-5 HCAPLUS

CN

Benzenepropanoic acid, 4-[2-[[6-amino-9-[N-ethyl-2,3-0-(1-methylethylidene)-.beta.-D-ribofuranuronamidosyl]-9H-purin-2-yl]amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-B

—OBu−t

RN 120225-77-6 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-[(2-phenylethyl)amino]-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 120225-75-4 120225-76-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of adenosinecarboxamide derivs. as CNS and cardiovascular agents)

RN 120225-75-4 HCAPLUS

CN .beta.-D-Ribofuranuronamide, l-(6-amino-2-chloro-9H-purin-9-yl)-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

# Absolute stereochemistry.

RN 120225-76-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[6-amino-9-[N-ethyl-2,3-O-(1-methylethylidene)-.beta.-D-ribofuranuronamidosyl]-9H-purin-2-yl]amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-B

---OBu−t

L35 ANSWER 41 OF 63 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1989:24223 HCAPLUS

DOCUMENT NUMBER:

110:24223

TITLE:

Conformational analysis of 8-substituted

isopropylidene derivatives of adenosine-5'-carboxylic

acid

AUTHOR(S):

SOURCE:

Timoshchuk, V. A.; Ermolenko, T. M.; Akhrem, A. A.

CORPORATE SOURCE:

Beloruss. Inst. Epidemiol. Mikrobiol., Minsk, USSR

Zhurnal Organicheskoi Khimii (1988), 24(6), 1214-20

CODEN: ZORKAE; ISSN: 0514-7492

DOCUMENT TYPE:

Russian

Journal LANGUAGE:

NMR data confirms that for 2',3'-O-isopropylidene derivs. of adenosine 5'-carboxylic acid the most probable conformation is C4'-endo, O4'-exo, and C1'-endo. Compds. of this series are characterized principally by a syn-conformation of the heterocycle around the N-glycosidic bond relative to the ribose fragment of the mols. CD data confirmed that conformations are stabilized by a spatial convergence of the N3 heterocyclic atom and the carboxyl group.

IT 101966-36-3 101966-40-9 101966-46-5

RL: PRP (Properties)

(conformation of, NMR and CD in relation to)

RN 101966-36-3 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-1-(6,8-diamino-9H-purin-9-yl)-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

RN 101966-40-9 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-8-(methylamino)-9H-purin-9-yl]-1-deoxy-N-methyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 101966-46-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-8-(dimethylamino)-9H-purin-9-yl]-1-deoxy-N-methyl-2,3-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L35 ANSWER 42 OF 63 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1986:627200 HCAPLUS

DOCUMENT NUMBER:

105:227200

TITLE:

Synthesis of uronic acid nucleosides. II. Synthesis

of 8-substituted adenosine-5'-carboxamides

AUTHOR(S): CORPORATE SOURCE: Akhrem, A. A.; Ermolenko, T. M.; Timoshchuk, V. A.

Beloruss. Nauchno-Issled. Inst. Epidemiol. Mikrobiol.,

Minsk, USSR SOURCE: Zhurnal Orga

Zhurnal Organicheskoi Khimii (1985), 21(8), 1800-5

CODEN: ZORKAE; ISSN: 0514-7492

DOCUMENT TYPE:

Journal

LANGUAGE:

Russian

GI

AB Amides of 8-substituted adenosine-5'-carboxylic acid were prepd. Starting from the Me ester of 8-bromo-2',3'-O-isopropylideneadenosine-5'-carboxylate and the Et ester of 8-bromoadenosine-5'-carboxylate were obtained the amide, methylamide, dimethylamide, and the ethylamide of the corresponding acid, which contained bromo-, amino, methylamino-, dimethylamino-, ethylamino-, and mercapto groups in position 8 of the adenine base. Thus, treating adenosine I (R = OMe, X = Br) with NH3 in MeOH at 18-25.degree. gave 82% I (R = NH2, X = Br). The selectivity of primary and secondary amines, on the ester group and 8-bromoadenine residue was demonstrated.

IT 101966-40-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and hydrolysis of)

RN 101966-40-9 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-8-(methylamino)-9H-purin-9-yl]-1-deoxy-N-methyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 101966-36-3P 101966-46-5P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

RN 101966-36-3 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-1-(6,8-diamino-9H-purin-9-yl)-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 101966-46-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-8-(dimethylamino)-9H-purin-9-yl]-1-deoxy-N-methyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L35 ANSWER 43 OF 63 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1984:56841 HCAPLUS

DOCUMENT NUMBER:

100:56841

TITLE:

Fibrinolytic formulations containing adenosine

derivatives

PATENT ASSIGNEE(S):

Tanabe Seiyaku Co., Ltd., Japan

SOURCE:

Jpn. Kokai Tokkyo Koho, 3 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND DATE

APPLICATION NO. DATE

PATENT NO.

Searched by Paul Schulwitz (703)305-1954

19831013

JP 58174324 - - A2 PRIORITY APPLN. INFO.:

JP 1982-58507 JP 1982-58507

19820407 19820407

NH2 **BuNHCO** R<sub>20</sub> ORI Ι

Formulations contg. I (R1 and R2 = propionyl or R1 + R2= AΒ methoxyethylidene) activate fibrinolysis. Thus, 2',3'-0dipropionyladenosine-5'-carboxylic acid butylamide(I) [88480-43-7] 70, D-mannitol 73, and corn starch 50 g were mixed using 5 g hydroxypropyl cellulose as binder, granulated, combined with 2 g Mg stearate, and made into tablets. I was prepd. by the acylation of adenosine-5'-carboxylic acid butylamide [35788-23-9] with propionic anhydride.

IT 62622-82-6P

RL: PREP (Preparation)

(prepn. of, for fibrinolysis activation)

62622-82-6 HCAPLUS RN

.beta.-D-Ribofuranuronamide, 1-(6-amino-9H-purin-9-yl)-N-butyl-1-deoxy-2,3-CN O-(1-methoxyethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L35 ANSWER 44 OF 63 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1984:26035 HCAPLUS

DOCUMENT NUMBER:

100:26035

TITLE:

Fibrinolytic formulations containing adenosine

derivatives

PATENT ASSIGNEE(S):

Tanabe Seiyaku Co., Ltd., Japan

SOURCE:

Jpn. Kokai Tokkyo Koho, 8 pp.

CODEN: JKXXAF

DOCUMENT TYPE: LANGUAGE:

Patent Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KI	ID DATE	APPLICATION NO.	DATE
JP 58174323 A2	19831013	JP 1982-58506	19820407
PRIORITY APPLN. INFO.:		JP 1982-58506	19820407

AB Fibrinolytic formulations contain I (R1 and R2 = H, alkanoyl, etc.; R3 = C1-3 alkylamino, alkenylamino, etc.). Thus, adenosine-5'-carboxylic acid cyclohexylamide [35788-32-0] was treated with Me orthoacetate [56893-90-4] to give 2',3'-0-methoxyethylideneadenosine-5'-carboxylic acid cyclohexylamide (II) [88255-85-0]. Tablets contg. 1% I were described. The min. effective oral dose for the hemolytic activity of II in rats was 30 mg/kg.

IT 62622-78-0P 88255-90-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and fibrinolytic activity of)

RN 62622-78-0 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-(6-amino-9H-purin-9-y1)-1-deoxy-N-ethyl-2,3-O-(1-methoxyethylidene)- (9CI) (CA INDEX NAME)

RN 88255-90-7 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-(6-amino-9H-purin-9-yl)-1-deoxy-2,3-0-(1methoxyethylidene)-N-2-propenyl- (9CI) (CA INDEX NAME)

# Absolute stereochemistry.

L35 ANSWER 45 OF 63 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER:

DOCUMENT NUMBER:

1980:215696 HCAPLUS

92:215696

TITLE:

N1,N6-Ethenoadenosine-5'-(N-ethyl carboxamide)

AUTHOR(S):

Prasad, Raj Nandan; Tietje, Karin

CORPORATE SOURCE:

Org. Chem. Res., Abbott Lab., Ltd., Montreal, QC, H4P

1A5, Can.

SOURCE:

Nucl. Acid Chem. (1978), Volume 2, 701-7. Editor(s):

Townsend, Leroy B.; Tipson, R. Stuart. Wiley: New

York, N. Y. CODEN: 42TBAU

DOCUMENT TYPE:

Conference

LANGUAGE:

GI

English

Ethenoadenosine I was prepd. by cyclization of adenosine II with ClCH2CHO. AΒ II was prepd. from acid III by 3 methods, e.g., by sequential chlorination with SOC12, amidation with EtNH2, and deisopropylidenation.

IT 39491-53-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and deisopropylidenation of)

39491-53-7 HCAPLUS RN

CN .beta.-D-Ribofuranuronamide, 1-(6-amino-9H-purin-9-yl)-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L35 ANSWER 60 OF 63 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1976:59956 HCAPLUS

DOCUMENT NUMBER:

84:59956

TITLE:

Adenosine-5'-carboxylic acid amides Stein, Herman Hal; Prasad, Raj N.

INVENTOR(S): PATENT ASSIGNEE(S):

Abbott Laboratories, USA

SOURCE:

U.S., 7 pp. Division of U.S. 3,864,483.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

#### PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
US 3914415	Α	19751021	US 1974-492950	19740730		
US 4029884	Α	19770614	US 1972-236980	19720322		
US 3864483	Α	19750204	US 1973-370084	19730614		
PRIORITY APPLN. INFO.	:		US 1971-125893	19710318		
			US 1972-236980	19720322		
			US 1973-370084	19730614		

GI For diagram(s), see printed CA Issue.

AB I (e.g., R1 = H, R2 = H, adamantyl, cyclopropyl, Et, PhOCH2CH2, allyl, 2,6-Me2C6H3, HOCH2CH2; R1 = R2 = allyl) (34 compds.), possessing cardiovascular and antiinflammatory activities, were prepd. by treatment of 2',3'-O-isopropylideneadenosine-5'-carboxylic acid chloride with R1R2NH followed by hydrolysis with 1N HC1.

IT 39491-51-5P 39491-53-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and deblocking of)

RN 39491-51-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-(6-amino-9H-purin-9-yl)-1-deoxy-N-methyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

#### Absolute stereochemistry.

RN 39491-53-7 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-(6-amino-9H-purin-9-yl)-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

IT 58048-27-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

RN 58048-27-4 HCAPLUS

.beta.-D-Ribofuranuronamide, 1-(6-amino-9H-purin-9-yl)-1-deoxy-2,3-0-(1-CN methylethylidene)-N-2-propenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L35 ANSWER 61 OF 63 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1976:44606 HCAPLUS

DOCUMENT NUMBER:

84:44606

TITLE:

Compounds for increasing coronary partial pressure of

oxygen in mammals

INVENTOR(S):

Stein, Herman Hal; Prasad, Raj N.

PATENT ASSIGNEE(S):

Abbott Laboratories, USA

SOURCE:

U.S., 7 pp. Division of U.S. 3,864,483.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

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US 3914414
                       Α
                            19751021
                                           US 1974-492949
                                                             19740730
     US 4029884
                       Α
                            19770614
                                           US 1972-236980
                                                             19720322
     US 3864483
                       Α
                            19750204
                                           US 1973-370084
                                                             19730614
     US 3966917
                       Α
                            19760629
                                           US 1975-590548
                                                             19750626
PRIORITY APPLN. INFO.:
                                        US 1971-125893
                                                            19710318
                                        US 1972-236980
                                                            19720322
                                        US 1973-370084
                                                            19730614
                                        US 1974-492949
                                                            19740730
```

Adenosine-5'-carboxamides, useful as antihypertensive agents, were prepd. AB by treating 2',3'-O-isopropylideneadenosine-5'-carbonyl chloride (I) with amines followed by acid hydrolysis. Thus, I with NH3 2 hr at -50.degree. gave 55% 2',3'-O-isopropylideneadenosine-5'-carboxamide (II). Treatment of II with 1N HCl at 60-70.degree. for 45 min gave adenosine-5'carboxamide.

IT 57872-94-3P 57872-95-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and antihypertensive activity of)

57872-94-3 HCAPLUS RN RN 57872-95-4 HCAPLUS

L35 ANSWER 62 OF 63 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1975:156656 HCAPLUS

DOCUMENT NUMBER:

82:156656

TITLE:

1,N6-Etheno-5'-adenosine carboxamides

INVENTOR(S):

Prasad, Raj N.; Garmaise, David L. Abbott Laboratories, USA

PATENT ASSIGNEE(S): SOURCE:

U.S., 3 pp.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3830796 US 3931401	A A	19740820 19760106	US 1972-317326 US 1974-472029	19721221 19740521
PRIORITY APPLN. INFO.	:		US 1972-317326	19740321

GT For diagram(s), see printed CA Issue.

Adenosines (I; R = Et, allyl, cyclobutyl), useful as antianginals and AB antihypertensives, were prepd. Thus, 2',3'-O-isopropylideneadenosine 5'-carboxylic acid chloride was treated with EtNH2 at -50 to -35.degree. to give the 5'-(N-ethylcarboxamide) which, treated 1 hr with 1N HCl, gave adenosine 5'-(N-ethylcarboxamide) II. Treatment of II with ClCH2CHO gave I (R = Et). The allyl and cyclobutyl derivs. were similarly prepd.

ΙT 39491-53-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

RN 39491-53-7 HCAPLUS

.beta.-D-Ribofuranuronamide, 1-(6-amino-9H-purin-9-yl)-1-deoxy-N-ethyl-2,3-CN O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

L35 ANSWER 63 OF 63 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1973:16454 HCAPLUS

DOCUMENT NUMBER:

78:16454

TITLE:

Adenosine-5'-carboxamides

INVENTOR(S):

Stein, Herman Hal; Prasad, Raj Nandan

PATENT ASSIGNEE(S): SOURCE:

Abbott Laboratories Ger. Offen., 12 pp.

CODEN: GWXXBX

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
DE 2213180 CA 1019727 GB 1386656 ZA 7201222 CH 551446 FR 2130364 SE 405363 SE 405363	A A1 A A A A5 C	19720928 19771025 19750312 19721129 19740715 19721103 19790315 19781204	DE 1972-2213180 CA 1972-135283 GB 1972-8446 ZA 1972-1222 CH 1972-3873 FR 1972-9349 SE 1972-3515	19720317 19720222 19720223 19720224 19720316 19720317		
PRIORITY APPLN. INFO.:	;		US 1971-125893	19710318		

GΙ For diagram(s), see printed CA Issue.

AΒ Four title compds. (I, R = H; R1 = NH2, NHMe, NMe2, and NHEt), useful in the treatment of angina pectoris and circulatory disturbances and as antihypertensives, were prepd. Chlorination of I (RR = CMe2, R1 = OH) with SOC12 to give I (RR = CMe2, R1 = C1), followed by treatment with amines, RlH, and hydrolysis with N HCl gave the corresponding title compd.

IT 39491-51-5P 39491-53-7P

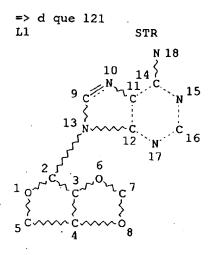
RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

RN39491-51-5 HCAPLUS

.beta.-D-Ribofuranuronamide, 1-(6-amino-9H-purin-9-yl)-1-deoxy-N-methyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

RN 39491-53-7 HCAPLUS

.beta.-D-Ribofuranuronamide, 1-(6-amino-9H-purin-9-yl)-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

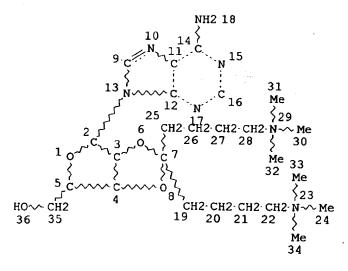


NODE ATTRIBUTES:
NSPEC IS RC AT 18
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

L2 3214 SEA FILE=REGISTRY SSS FUL L1 L20 STR



NODE ATTRIBUTES:
CONNECT IS E2 RC AT 9
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 36

=> d que 129
L1 STR

N 18

10 14

9 c N 11 C N 15

13 N C C N

12 N 16

10 C 7

6 10 C 7

NODE ATTRIBUTES:

NSPEC IS RC AT 18
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

L2 3214 SEA FILE=REGISTRY SSS FUL L1 L22 36416 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERTENSION/CT L25 5576 SEA FILE=HCAPLUS ABB=ON PLU=ON ISCHEMIA+OLD/CT L26 2613 SEA FILE=HCAPLUS ABB=ON PLU=ON ANTI-ISCHEMIC AGENTS/CT L27 4987 SEA FILE=HCAPLUS ABB=ON PLU=ON VASODILATION/CT L28 8845 SEA FILE=HCAPLUS ABB=ON PLU=ON VASODILATORS/CT L29 39 SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND (L22 OR HYPERTENS? OR L25 OR L26 OR ISCHEM? OR L27 OR L28 OR VASODIL? OR SYMPATHET?(2 A) BLOCK? OR PROPHYLACT?)

# => d ibib abs hitstr 129 1-39

L29 ANSWER 1 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

2002:332678 HCAPLUS

DOCUMENT NUMBER:

136:350561

TITLE:

Use of P2Y12 receptor antagonists as platelet

aggregation inhibitors

INVENTOR(S):

Boyer, Jose L.; Olins, Gillian M.; Yerxa, Benjamin R.;

Douglass, James G.

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 43 pp., Cont.-in-part of U.S.

Ser. No. 643,138.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

. 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002052337	Al	20020502	US 2001-934970	20010821
US 2002128224	<b>A</b> 1	20020912	US 2002-87551	20020227
US 2003008834	A1	20030109	US 2002-82998	20020227
PRIORITY APPLN. INFO.	:		US 2000-643138 A2	20000821
			US 2001-934970 A2	20010821

OTHER SOURCE(S): MARPAT 136:350561

The invention discloses a method of preventing or treating diseases or conditions assocd. with platelet aggregation and treating thrombosis. The method involves administering to a subject a pharmaceutical compn. comprising a therapeutic effective amt. of P2Y12 receptor antagonist compd., to bind the P2Y12 receptors on platelets and inhibit ADP-induced platelet aggregation. The P2Y12 receptor antagonist compds. disclosed include mononucleoside polyphosphates and dinucleoside polyphosphates.

IT 401619-32-7 401619-52-1 401619-57-6 401620-06-2 420131-31-3 420131-40-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(P2Y12 receptor antagonists as platelet aggregation inhibitors)

RN 401619-32-7 HCAPLUS

CN Adenosine 5'-(trihydrogen diphosphate), 2',3'-O-(2-phenylethylidene)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 401619-52-1 HCAPLUS

CN Adenosine 5'-(pentahydrogen tetraphosphate), 2',3'-O-(2-phenylethylidene)-, P'''.fwdarw.5'-ester with uridine (9CI) (CA INDEX NAME)

PAGE 1-B

RN 401619-57-6 HCAPLUS

CN Adenosine 5'-(pentahydrogen tetraphosphate), 2',3'-0-(2-phenylethylidene)-, P'''.fwdarw.5'-ester with 2',3'-0-(2-phenylethylidene)uridine (9CI) (CA INDEX NAME)

PAGE 1-B

\_\_\_ Ph

PAGE 2-A

0

RN 401620-06-2 HCAPLUS

CN Adenosine, N-[2-(methylthio)ethyl]-2',3'-0-(2-phenylethylidene)-2-[(3,3,3-trifluoropropyl)thio]-, 5'-[hydrogen (difluorophosphonomethyl)phosphonate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 420131-31-3 HCAPLUS

CN Adenosine 5'-(pentahydrogen tetraphosphate), 2',3'-O-(2-phenylethylidene)-, P'''.fwdarw.5'-ester with adenosine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

RN 420131-40-4 HCAPLUS

CN Adenosine 5'-(pentahydrogen tetraphosphate), N-[2-(methylthio)ethyl]-2',3'-O-(2-phenylethylidene)-2-[(3,3,3-trifluoropropyl)thio]-,
P'''.fwdarw.5'-ester with 2',3'-O-(2-phenylethylidene)adenosine (9CI) (CA INDEX NAME)

PAGE 1-B

L29 ANSWER 2 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

2002:271942 HCAPLUS

DOCUMENT NUMBER:

136:291358

TITLE:

Diagnostic uses of 2-substituted adenosine

carboxamides

INVENTOR(S):

Leung, Edward

PATENT ASSIGNEE(S):

King Pharmaceuticals Research and Development, Inc.,

SOURCE:

U.S., 17 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
US 6368573	B1	20020409	US 1999-440330	19991115		
PRIORITY APPLN. INFO.:	:	US	1999-440330	19991115		
OTHER SOURCE(S):	MA	RPAT 136:291358				

The invention concerns a method for measuring myocardial function in a AB mammal in need of such measurement by: (a) administering 2-substituted adenosine carboxamide derivs. at a dosage rate of less than 1 .mu.g/kg/min, preferably between about 0.01 and 1 .mu.g/kg/min; and then: (b) performing a technique on the mammal to detect myocardial function. The method can be used to diagnose myocardial dysfunction by electrophysiol. anal. or by imaging the vasculature of the heart, esp. under conditions that simulate stress.

TΤ 120225-76-5

> RL: ADV (Adverse effect, including toxicity); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(diagnostic uses of 2-substituted adenosine carboxamides)

120225-76-5 HCAPLUS RN

Benzenepropanoic acid, 4-[2-[6-amino-9-[N-ethyl-2,3-0-(1-amino-9-[N-CN methylethylidene) -. beta. -D-ribofuranuronamidosyl] -9H-purin-2yl]amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-B

∠ OBu−t

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

2001:904207 HCAPLUS

DOCUMENT NUMBER:

136:37902

TITLE:

Preparation of 2-aminocarbonyl-9H-purine nucleosides and their uses in treatment of respiratory disease, as

A2a receptor agonists and anti-inflammatory agents

Mantell, Simon John; Stephenson, Peter Thomas

INVENTOR(S):

Pfizer Limited, UK; Pfizer Inc.

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 198 pp.

DOCUMENT TYPE:

CODEN: PIXXD2 Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

MILY ACC. NOM. COUNT: 1

PATENT INFORMATION:

PATENT NO.				KIND DATE			APPLICATION NO.						DATE				
									_								
WO	2001	0943	68	Α	1	2001	1213		W	0 20	01-I	в973		2001	0605		
	W:	AE,	AG.	AL.	AM.	AT.	AU.	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
		co.	CR.	CU.	CZ.	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM.	HR.	HU.	ID.	IL,	IN.	IS.	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
						MA.											

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RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                                                 US 2001-874007
                                                                                            20010605
                                          20020516
       US 2002058641
                                  A1
                                                                  EP 2001-934242
                                          20030319
                                                                                            20010605
       EP 1292604
                                   A1
             R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                                                             GB 2000-14048
                                                                                       A 20000606
PRIORITY APPLN. INFO.:
                                                                                       A 20000725
                                                             GB 2000-18246
                                                                                       A 20001011
                                                             GB 2000-24920
                                                             US 2000-214307P P 20000627
                                                             US 2000-225236P P 20000815
                                                             US 2000-245243P P 20001102
                                                             WO 2001-IB973
                                                                                       W 20010605
OTHER SOURCE(S):
                                     MARPAT 136:37902
```

- \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY AVAILABLE VIA OFFLINE PRINT \*
- 2-Aminocarbonyl-9H-purine nucleosides I wherein R, R2 are independently H, AB alkyl; R1 is H, substituted alkyl, fluorenyl; R3 is H, alkyl, cycloalkyl, benzyl; R4 is substituted azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl; R3R4 taken together with the nitrogen atom to which they are attached, represent azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopiperidinyl or homopiperazinyl, each being optionally substituted on a ring nitrogen or carbon atom by alkyl or cycloalkyl; R5 is CH2OH, amide; X is substituted alkylene; RX or R2X with the nitrogen atom to which they are attached , represent azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl; Y is CO, CS, SO2, C=N(CN); were prepd. as A2a receptor agonists and anti-inflammatory agents. Thus, nucleoside II was prepd. and tested as A2a receptor agonist and anti-inflammatory agent. Title compds. were tested for biol. activity as A2a receptor agonists and anti-inflammatory agents and all were found to have an IC50 of less than 100 nM.
- IT 380222-88-8P 380222-90-2P 380222-92-4P 380222-93-5P 380222-94-6P
  - RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
    - (prepn. of 2-aminocarbonyl-9H-purine nucleosides and uses in treatment of respiratory disease, as A2a receptor agonists and anti-inflammatory agents)
- RN 380222-88-8 HCAPLUS
- CN 9H-Purine-2-carboxylic acid, 6-[(2,2-diphenylethyl)amino]-9-[2,3-O-(1-methylethylidene)-.beta.-D-ribofuranosyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 380222-90-2 HCAPLUS

CN .beta.-D-Ribofuranuronic acid, 1-deoxy-1-[6-[(2,2-diphenylethyl)amino]-2-(ethoxycarbonyl)-9H-purin-9-yl]-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

# Absolute stereochemistry.

RN 380222-92-4 HCAPLUS

CN 9H-Purine-2-carboxylic acid, 6-[(2,2-diphenylethyl)amino]-9-[N-ethyl-2,3-0-(1-methylethylidene)-.beta.-D-ribofuranuronamidosyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 380222-93-5 HCAPLUS

CN 9H-Purine-2-carboxylic acid, 6-[(2,2-diphenylethyl)amino]-9-[N-ethyl-2,3-0-(1-methylethylidene)-.beta.-D-ribofuranuronamidosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 380222-94-6 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-1-[6-[(2,2-diphenylethyl)amino]-2[[[2-[[[[1-(2-pyridinyl)-4-piperidinyl]amino]carbonyl]amino]ethyl]amino]ca
rbonyl]-9H-purin-9-yl]-N-ethyl-2,3-0-(1-methylethylidene)- (9CI) (CA
INDEX NAME)

PAGE 1-B



REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

14

L29 ANSWER 4 OF 39 HCAPLUS COPYRIGHT 2003 ACS

2

ACCESSION NUMBER:

2000:911265 HCAPLUS

DOCUMENT NUMBER:

134:66148

TITLE:

Induction of pharmacological stress with

alkynyladenosine A2A adenosine receptor agonists

INVENTOR(S):

Linden, Joel M.; Glover, David K.; Beller, George A.;

MacDonald, Timothy

PATENT ASSIGNEE(S):

University of Virginia Patent Foundation, USA

SOURCE:

PCT Int. Appl., 36 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA!								APPLICATION NO.						DATE			
	WO 2000078774 A2 20001228 WO 2000078774 A3 20010712												2000	0612			
WO																	
	W:		•	•	•		-	•	•				-	CA,	-	-	
		CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GΕ,	GH,	GM,	HR,	ΗU,
		ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,
		LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,
		SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,
		ZW,	AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM						
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,
		DE,	DK,	ES,	FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,
						GΑ,											
BR	2000	0117	25 <sup>°</sup>	Ā	•	2002	0326		B	R 20	00-1	1725		2000	0612		
EP	1194	440		A.	2	2002	0410		E	P 20	00-9	4133	5	2000	0612		
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
						FI,		·									
JР	2003	•	•		•				J	P 20	01-5	0493	9	2000	0612		
	2001																

PRIORITY APPLN. INFO.:

US 1999-336198 A 19990618

WO 2000-US16029 W 20000612

OTHER SOURCE(S):

MARPAT 134:66148

AB A method is provided employing alkynyladenosine A2A adenosine receptor agonists as **vasodilators** to detect the presence and assess the severity of coronary artery stenosis. Prepn. of alkynyladenosine derivs. is also described.

IT 141018-25-9P 141018-26-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction; alkynyladenosine A2A adenosine receptor agonist for induction of pharmacol. stress and diagnosis of coronary artery stenosis)

RN 141018-25-9 HCAPLUS

CN Adenosine, 2-iodo-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141018-26-0 HCAPLUS

CN .beta.-D-Ribofuranuronic acid, 1-(6-amino-2-iodo-9H-purin-9-yl)-1-deoxy-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L29 ANSWER 5 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: DOCUMENT NUMBER:

1998:34074 HCAPLUS

128:188277

TITLE:

Adenosine receptor agonists: synthesis and biological

evaluation of the diastereoisomers of

2-(3-hydroxy-3-phenyl-1-propyn-1-yl)NECA

AUTHOR(S):

Camaioni, Emidio; Di Francesco, Emanuela; Vittori,

Sauro; Volpini, Rosaria; Cristalli, Gloria

CORPORATE SOURCE:

Dipartimento di Scienze Chimiche, Universita di

Camerino, Camerino, 62032, Italy

SOURCE:

Bioorganic & Medicinal Chemistry (1997), 5(12),

2267-2275

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER:

Elsevier Science Ltd.

DOCUMENT TYPE:

Journal

LANGUAGE: English

Among the recently reported 2-(ar)alkynyl derivs. of 5'-Nethylcarboxamidoadenosine (NECA), the (R,S)-2-(3-hydroxy-3-phenyl-1-propyn-1-yl)NECA [(R,S)-PHPNECA or SCH 59761] was found to be a very potent agonist at A1 and A2A receptor subtypes, with a Ki of 2.5 nM and 0.9 nM, resp. Furthermore, this compd. showed an inhibitory activity on platelet aggregation 16-fold higher than NECA, being the most potent anti-aggregatory nucleoside reported so far. Since this compd. bears a chiral carbon in the side chain, the diastereoisomer sepn. was undertaken both by chiral HPLC and by a stereospecific synthetic method. Binding assays have shown that the (S)-diastereomer is about fivefold more potent and selective than the (R)-diastereomer as agonist of the A2A receptor subtype [(S)-PHPNECA, KiA2A = 0.5 nM; (R)-PHPNECA, KiA2A = 2.6 nM]. Functional studies indicated that (S)-PHPNECA possesses marked vasodilating activity and produces a relevant decrease in heart rate. Moreover, the (S)-diastereomer proved to be about ten times more potent than the (R)-diastereomer in inducing cardiovascular effects, in in vivo hemodynamic studies. However, the greatest difference between these two enantiomers resulted in the platelet aggregation test: in fact, the (R)-diastereomer displayed an inhibitory activity similar to that of NECA, whereas the (S)-diastereomer was 37-fold more active than NECA as an inhibitor of rabbit platelet aggregation, induced by ADP. These data suggest that (S)-PHPNECA could be a useful tool to investigate the mode of binding of agonists to the platelet adenosine receptor subtype.

203794-22-3P 203794-23-4P ΤT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and biol. evaluation of diastereoisomers of 2-(3-hydroxy-3-phenyl-1-propyn-1-yl)NECA as adenosine receptor agonists)

203794-22-3 HCAPLUS RN

.beta.-D-Ribofuranuronamide, 1-[6-amino-2-[(35)-3-[[[(1R)-1-(1-CN naphthalenyl)ethyl]amino]carbonyl]oxy]-3-phenyl-1-propynyl]-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 203794-23-4 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-[(3R)-3-[[[[(1R)-1-(1-naphthalenyl)ethyl]amino]carbonyl]oxy]-3-phenyl-1-propynyl]-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

PAGE 1-B

#### IT 162936-24-5

RL: RCT (Reactant); RACT (Reactant or reagent)
 (synthesis and biol. evaluation of diastereoisomers of
2-(3-hydroxy-3-phenyl-1-propyn-1-yl)NECA as adenosine receptor
agonists)

RN 162936-24-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-(6-amino-2-iodo-9H-purin-9-yl)-1-deoxy-N-ethyl-2,3-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

### IT 203794-21-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. evaluation of diastereoisomers of 2-(3-hydroxy-3-phenyl-1-propyn-1-yl)NECA as adenosine receptor agonists)

RN 203794-21-2 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(3-hydroxy-3-phenyl-1-propynyl)-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 6 OF 39 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1997:761605 HCAPLUS

DOCUMENT NUMBER:

128:34983

TITLE:

SOURCE:

Preparation of nucleosides as A3 adenosine receptor

agonists

INVENTOR(S):

Jacobson, Kenneth A.; Jeong, Heaok Kim; Siddiqi, Suhaib M.; Johnson, Carl R.; Secrist, John A., III;

Tiwari, Kamal N.

PATENT ASSIGNEE(S):

United States Dept. of Health and Human Services, USA U.S., 35 pp., Cont.-in-part of U.S. Ser. No. 274,628.

CODEN: USXXAM

DOCUMENT TYPE:

PE: Patent English

LANGUAGE: En FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO. DA	TE
US 5688774	Α	19971118	US 1995-396111 19	950228
US 5773423	Α	19980630	US 1994-274628 19	940713
PRIORITY APPLN.	INFO.:		US 1993-91109 B2 19	930713
			US 1993-163324 B2 19	931206
			US 1994-274628 A2 19	940713

OTHER SOURCE(S):

MARPAT 128:34983

GI

AB Title nucleosides I (R = H, Y; R1 = benzyl, halobenzyl; R2 = H, halo, alkylamino; X1 = H, alkyl; X2 = alkylamido; X3, X4 = independently H, OH,

NH2, N3, halo, Bz) were prepd. as A3 adenosine receptor agonists. The present invention also provides a method of selectively activating an A3 adenosine receptor in a mammal, which method comprises acutely or chronically administering to a mammal in need of selective activation of its A3 adenosine receptor a therapeutically or **prophylactically** effective amt. of a compd. which binds with the A3 receptor so as to stimulate an A3 receptor-dependent response. Thus, N3-(3-iodobenzyl)-9-Me adenine was prepd. and showed an affinity at rat brain adenosine receptors (Ki = 2.23-48.3 .mu.M).

IT 163042-89-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of nucleosides as a adenosine receptor agonists)

RN 163042-89-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[2-chloro-6-[[(3-iodophenyl)methyl]amino]-9H-purin-9-yl]-1-deoxy-N-methyl-, cyclic 2,3-carbonothioate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 170966-20-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of nucleosides as a adenosine receptor agonists)

RN 170966-20-8 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-[[(3-aminophenyl)methyl]amino]-9H-purin-9-yl]-1-deoxy-N-methyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

L29 ANSWER 7 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1997:12370 HCAPLUS

DOCUMENT NUMBER:

126:75189

TITLE:

Preparation of N6-(phenylalkyl) adenosine derivatives having selective affinity to adenosine A3 receptor Mitsuya, Morihiro; Takeshita, Hiroshi; Ihara, Masaki

INVENTOR(S): Mitsuya, Morihiro; Takeshit

PATENT ASSIGNEE(S): SOURCE:

Banyu Pharma Co Ltd, Japan Jpn. Kokai Tokkyo Koho, 12 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
					<del></del>
JP 08269083 PRIORITY APPLN. INFO.	. A2	19961015	JP.	JP 1995-101772 1995-101772	19950403 19950403
OTHER SOURCE(S):	_	RPAT 126:751		1333 101/12	13300100

The title compds. (I; Ar = Ph, arom. heterocyclyl; Q = lower alkylene; R1 AB = Cl, lower alkyl, alkoxy, or alkylthio, NR4R5; wherein R4 , R5 = H, lower alkyl; R2 = HOCH2, H2NCO, N-alkylcarbamoyl; R3 = H, OH, NH2, lower alkoxy) or pharmaceutically acceptable salts thereof, which have reduced side effects, are prepd. A remedy for hypertension, unstable angina pectoris, acute myocardial infarction, and/or brain nerve disorders contg. I is claimed. Thus, 1-(2,6-dichloro-9H-purin-9-yl)-2,3-0-isopropylidene-.beta.-D-ribofuranuronic acid (prepn. given) was condensed with 3-(2-thiazolyl)benzylamine hydrochloride (prepn. given) in EtOH at room temp. for 15 h and then with methylamine using 1-ethyl-3-(3dimethylaminopropyl)carbodiimide hydrochloride in CHCl3, followed by treatment with aq. 85% HCO2H, to give the title compd. (II). II showed Ki (competitive binding inhibition const.) of 6,990 and 1.00 for adenosine Al receptor prepn. from rat homogenized brain and adenosine A3 receptor of Rat basophilic leukemia mast cells (RBL-2H3), resp.

I

IT 184847-93-6P 184847-94-7P 184847-95-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of N6-(phenylalkyl) adenosine derivs. having selective affinity to adenosine A3 receptor for disease treatment)

RN 184847-93-6 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[2-chloro-6-[[[3-(2-thiazolyl)phenyl]methyl]amino]-9H-purin-9-yl]-1-deoxy-N-methyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

RN 184847-94-7 HCAPLUS

.beta.-D-Ribofuranuronic acid, 1-[2-chloro-6-[[3-(2-thiazolyl)phenyl]methyl]amino]-9H-purin-9-yl]-1-deoxy-2,3-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 184847-95-8 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-methyl-1-[2-(methylamino)-6-[[[3-(2-thiazolyl)phenyl]methyl]amino]-9H-purin-9-yl]-2,3-O-(1-methylethylidene)-(9CI) (CA INDEX NAME)

# Absolute stereochemistry.

L29 ANSWER 8 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1996:616599 HCAPLUS

DOCUMENT NUMBER:

125:317355

TITLE:

Preparation of adenosine derivatives having antihypertensive, cardioprotective, anti-

ischemic and antilipolytic properties

INVENTOR(S):

Spada, Alfred P.; Fink, Cynthia A.; Myers, Michael R.

PATENT ASSIGNEE(S):

SOURCE:

Rhone-Poulenc Rorer Pharmaceuticals Inc., USA U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 229,882,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PA:	rent :	NO.		KI	ND	DATE			A	PPLI	CATI	ON NO	o.	DATE			
US	5561	134		A		1996	1001		U	5 19	94-3	1676	1	1994	1003		
บร	5364	862		Α		1994:	1115		U	s 19	92-9	5578	3	1992	1002		
CA	2188	147		A.	A	1995	1026		C	A 19	95-2	1881	47	1995	0419		
CA	2188	147		С		2001	0403										
WO	9528	160		Α	1	1995	1026		W	) 19	95-U	S480	0	1995	0419		
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		MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	ТJ,	TT,
		UA,	ŪĞ														
	RW:	KE,	MW,	SD,	SZ,	UG,	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙĒ,	IT,
		LU,	MC,	NL,	PT,	SE,	BF,	BJ,	CF,	CG,	CI,	CM,	GA,	GN,	ML,	MR,	NE,
		SN,	TD,	TG		-	•	•						•			
ΑU	9522	949	•	A	1	1995	1110		Αl	J 19	95-2	2949		1995	0419		

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AU 684635
                            19971218
                       B2
     EP 758897
                            19970226
                                            EP 1995-916451
                                                             19950419
                       Α1
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
     CN 1148811
                       Α
                            19970430
                                            CN 1995-193170
                                                             19950419
     CN 1086704
                            20020626
                                            HU 1996-2829
     HU 75331
                       A2
                            19970528
                                                             19950419
                                                             19950419
                                            BR 1995-7327
     BR 9507327
                       Α
                            19971007
                                            JP 1995-527171
                                                             19950419
     JP 09512020
                       Т2
                            19971202
                                            EP 2000-103467
                                                             19950419
     EP 1006115
                       A2
                            20000607
                       A3
                            20000628
     EP 1006115
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE
                                           RU 1996-121567
                                                             19950419
     RU 2166319
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                            20010510
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                                           NZ 1995-284357
                                                             19950419
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                                                             19950419
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                                            PL 1995-316961
                                                             19950419
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                                           US 1995-455361
                                                             19950531
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                       Α
                            19980407
     US 5652366
                       Α
                            19970729
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                                                             19950607
                            19961018
                                            NO 1996-4438
                                                             19961018
     NO 9604438
                       Α
                                            FI 1996-4218
     FI 9604218
                            19961217
                                                             19961018
                                            CZ 2001-2885
                                                             20010808
     CZ 290897
                       В6
                            20021113
                                                          B2 19900925
PRIORITY APPLN. INFO .:
                                        US 1990-587884
                                        US 1992-955783
                                                          A2 19921002
                                        US 1994-229882
                                                          B2 19940419
                                        US 1994-316761
                                                          A 19941003
                                         CZ 1996-3032
                                                          A3 19950419
                                         EP 1995-916451
                                                          A3 19950419
                                                          W 19950419
                                         WO 1995-US4800
OTHER SOURCE(S):
                         MARPAT 125:317355
```

NHX (Y) aZ

N

N

N

GΙ

OR5 OR6

Ι

The adenosine derivs. I [K = N or NO; Q = CH2 or O; T = R1R2NCO or R3OCH2; X = (un)substituted alkylene, cycloalkylene or cycloalkenylene Y = NR4, O or S; a = 0 or 1; Z = substituted pyrrolyl, pyrazolyl, indolyl, etc.; R1-5 = H, alkyl, aryl or heterocyclyl; R5,R6 = H, alkyl, aralkyl, etc.] are prepd. as antihypertensive, cardioprotective, antiischemic, and antilipolytic agents.

IT 165115-09-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(intermediate in prepn. of adenosine deriv. drug)

RN 165115-09-3 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)-1-[6-[[6-(2-thienyl)-3-cyclohexen-1-yl]amino]-9H-purin-9-yl]- (9CI) (CA INDEX NAME)

# Absolute stereochemistry.

L29 ANSWER 9 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1995:997439 HCAPLUS

DOCUMENT NUMBER:

124:202956

TITLE:

Preparation of adenosine derivatives having antihypertensive, cardioprotective, anti-

ischemic and antilipolytic properties.

INVENTOR (S):

Spada, Alfred P.; Fink, Cynthia A.; Myers, Michael R.

PATENT ASSIGNEE(S):

Rhone-Poulenc Rorer Pharmaceuticals Inc., USA

SOURCE:

PCT Int. Appl., 75 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	ENT	NO.		KI	ND	DATE			<b>A</b> :	PPLI	CATI	ON N	o. 	DATE			
WO	9528	160		A	1	1995	1026		W	0 19	95 <b>-</b> U	5480	0	1995	0419		
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		GE,	HU,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LK,	LR,	LT,	LU,	LV,	MD,	MG,
		MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	ТJ,	TT,
		UA,															
	RW:	KE,	MW,	SD,	SZ,	UG,	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IE,	IT,
		LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	ML,	MR,	ΝE,
		SN,	TD,	TG													
US	5561	134		Α		1996	1001		U	s 19	94-3	1676	1	1994	1003		
ΑU	9522	949		Α	1	1995	1110		A	U 19	95-2	2949		1995	0419		
ΑU	6846	35		В	2	1997	1218										

EP	7588	9.7		A:	1 19	9702	226		EP	19	95-9	1645	1	1995	0419		
	R:	ΑT,	BE,	CH,	DE, D	K, E	ES,	FR,	GB,	GR,	IE,	IT,	LI,	LU,	NL,	PT,	SE
BR	9507	327		Α	19	9710	07		BR	19	95-7	327		1995	0419		
JP	0951	2020		T	2 19	9712	202		JP	19	95-5	2717	1	1995	0419		
RU	2166	319		C	2 20	0105	10		RU	19	96-1	2156	7	1995	0419		
NZ	2843	57		Α	20	0106	29		NZ	19	95-2	8435	7	1995	0419		
PL	1829	42		B1	L 20	0205	31		PL	19:	95-3	1696	1	1995	0419		
NO	9604	438		Α	19	9610	18		NO	19	96-4	438		1996	1018		
FI	9604	218		Α	19	9612	17		FI	19	96-42	218		1996	1018		
PRIORITY	( APP	LN. 1	INFO.	:				U	s 19	94-2	2298	82	Α	1994	0419		
								ប	S 19	94-3	3167	61	A	1994	1003		
								U	S 19	90-	58788	84	В2	1990	0925		
								U	S 19	92-	95578	83	<b>A</b> 2	1992	1002		
			-					W	0 19	95−≀	JS480	00	W	1995	0419		
OMITTO OC		101			***	- 10			_								

OTHER SOURCE(S):

MARPAT 124:202956

GI

$$Q^{1=} (z^2)_n$$

$$Z^1 \downarrow_{R^9}$$

$$Q^{2=} Z^1 \downarrow_{(z^2)_n}$$

$$Q^{2=} Z^1 \downarrow_{(z^2)_n}$$

AB Title compds. [I; K = N, NO, CH; Q = CH2, O; T = R3R4NCO, R5OCH2; X = (substituted) alkylene, cycloalkylene, cycloalkenylene; Y = NR6, O, S; a = 0, 1; R1, R2 = H, alkyl, aralkyl, carbamoyl, acyl, alkoxycarbonyl, aralkoxycarbonyl, aryloxycarbonyl; R1R2 = CO, CS, etc.; R3-R8 = H, alkyl, aryl, heterocyclyl; Z = Q1, Q2; Z1 = N, CR7, (CH)mC5, (CH)mN; m = 1, 2; Z2 = N, NR8, O, S; n = 0, 1; R9, R10 = H, OH, alkyl, hydroxyalkyl, alkylmercapto, thioalkyl, alkoxy, amino, acyl, halo, carbamoyl, etc.], were prepd. Thus, trans-2-(2-thienyl)cyclohex-4-enylamine, 6-chloropurine, and Et3N were refluxed in EtOH to give N6-[trans-2-(2-thienyl)-cyclohex-4-enyl]adenosine. The latter bound to adenosine A1 and A2 receptors with IC50 = 1.66 nM and 55 nM, resp., and induced vasorelaxation in swine coronary artery with IC50 = 0.73 .mu.M.

IT 173935-07-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of adenosine derivs. having antihypertensive, cardioprotective, anti-ischemic and antilipolytic properties)

RN 173935-07-4 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)-1-[6-[[6-(2-thienyl)-3-cyclohexen-1-yl]amino]-9H-purin-9-yl]-, (1S-trans)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L29 ANSWER 10 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1995:837438 HCAPLUS

DOCUMENT NUMBER:

123:257265

TITLE:

Preparation of N6-benzyladenosine-5'-uronamides,

modified xanthine ribosides, and related compounds as

adenosine A3 receptor agonists.

INVENTOR(S):

Jacobson, Kenneth A.; Gallo-Rodriguez, Carola; Von Galen, Philip J. M.; Von Lubitz, Dag K. J. E.; Jeong,

Heaok Kim

PATENT ASSIGNEE(S):

United States Dept. of Health and Human Services, USA

PCT Int. Appl., 175 pp.

SOURCE:

PCI Inc. Appi., 175 pp

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
WO 9502604	Al 19950126	WO 1994-US7835	19940713
W: AU, CA,	JP		
RW: AT, BE,	CH, DE, DK, ES,	FR, GB, GR, IE, IT, LU,	MC, NL, PT, SE
AU 9473310	A1 19950213	AU 1994-73310	19940713
EP 708781	A1 19960501	EP 1994-923445	19940713
EP 708781	B1 20011004		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE AT 206432 E 20011015 AT 1994-923445 19940713 PRIORITY APPLN. INFO.: US 1993-91109 A 19930713

US 1993-163324 A 19931206 WO 1994-US7835 W 19940713

OTHER SOURCE(S): MARPAT 123:257265

Ι

ĠI

Title compds. [I; R1 = RaRbNCO, HORc; Ra, Rb = H, alkyl, amino, haloalkyl, AB aminoalkyl, cycloalkyl, BOC-aminoalkyl; RaRbN = heterocyclyl; Rc = alkyl, amino, haloalkyl, aminoalkyl, cycloalkyl, BOC-aminoalkyl; R2 = H, halo, alkyl ether residue, amino, alkylamino, alkenyl, alkynyl, thio, alkylthio; R3 = (R) - and (S) - 1 - phenylethyl, (substituted) PhCH2, substitutedphenylethyl] and related compds., were prepd. Thus, 2-chloro-N6-(3iodobenzyl) adenine was refluxed with hexamethyldisilazane and cat. (NH4)2SO4 to give a silyl deriv. which was refluxed with N-Me I-O-acetyl-2, 3-dibenzoyl-.alpha.,.beta.-D-ribofuronamide and trimethylsilyl triflate in dichloroethane to give 2-chloro-N6-(3iodobenzyl)-9-[5-(methylamido)-2,3-di-O-benzoyl-.beta.-Dribofuranosyl]adenine. The latter was stirred with NH3 in MeOH for 16 h  $\,$ to give 68.7% 2-chloro-N6-(3-iodobenzyl)-9-[5-(methylamido)-.beta.-Dribofuranosyl]adenine. This showed Ki = 0.23 nM in a radioligand binding assay at rat brain A3 receptors.

IT 362-75-4, 2',3'-Isopropylideneadenosine

RL: RCT (Reactant); RACT (Reactant or reagent) (prepn. of N6-benzyladenosine-5'-uronamides, modified xanthine ribosides, and related compds. as adenosine A3 receptor agonists)

RN 362-75-4 HCAPLUS

CN Adenosine, 2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

IT 19234-66-3P 23754-29-2P 152918-54-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of N6-benzyladenosine-5'-uronamides, modified xanthine ribosides, and related compds. as adenosine A3 receptor agonists)

RN 19234-66-3 HCAPLUS

CN .beta.-D-Ribofuranuronic acid, 1-(6-amino-9H-purin-9-yl)-1-deoxy-2,3-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 23754-29-2 HCAPLUS

CN .beta.-D-Ribofuranuronic acid, 1-(6-amino-9H-purin-9-yl)-1-deoxy-2,3-0-(1-methylethylidene)-, methyl ester (9CI) (CA INDEX NAME)

RN 152918-54-2 HCAPLUS

CN Benzenesulfonic acid, 4-[[[9-[N-methyl-2,3-O-(1-methylethylidene)-.beta.-D-ribofuranuronamidosyl]-9H-purin-6-yl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L29 ANSWER 11 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1995:508300 HCAPLUS

DOCUMENT NUMBER:

122:291434

TITLE:

2-Aralkynyl and 2-Heteroalkynyl Derivatives of Adenosine-5'-N-Ethyluronamide as Selective A2a

Adenosine Receptor Agonists

AUTHOR(S):

Cristalli, Gloria; Camaioni, Emidio; Vittori, Sauro;

Volpini, Rosaria; Borea, Pier Andrea; Conti, Annamaria; Dionisotti, Silvio; Ongini, Ennio;

Monopoli, Angela

CORPORATE SOURCE:

Dipartimento di Scienze Chimiche, Universita di

Camerino, Camerino, 62032, Italy

SOURCE:

Journal of Medicinal Chemistry (1995), 38(9), 1462-72

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE: LANGUAGE: Journal English

GI

AR A series of new 2-aralkynyl and 2-heteroaralkynyl derivs. of 5'-(N-carboxamido)adenosine NECA, e.g. I [R = H, Ph, C6H4R1-4, 2-pyridyl, 2-furyl, 2-thiazolyl; R1 = Me, OMe, OH, NH2, F], were synthesized and studied in binding and functional assays to assess their potency for the A2a compared to A1 adenosine receptors. Compds. bearing an arom. or heteroarom. ring, conjugated to the triple bond, showed generally weaker activity at the A2a receptor and lower selectivity (A2a vs A1) than the alkylalkynyl derivs. previously reported. However, the (4-formylphenyl)ethynyl deriv. showed affinity in the low nanomolar range and high selectivity (about 160-fold) for the A2a receptor. The presence of heteroatoms improved vasorelaxant activity, I (R = 2-thiazolyl) being the most potent in the series. Introduction of methylene groups between the triple bond and the Ph ring favored the A2a binding affinity, and the 5-phenyl-1-pentynyl deriv. was found to be highly potent and selective (about 180-fold) at A2a receptors. With regard to platelet activity, the presence of arom. or heteroarom. rings decreased the potency in comparison with that of NECA and of N-ethyl-1'-deoxy-1'-(6-amino-2-hexynyl-9H-purin-9yl)-.beta.-D-ribofuranuronamide (HENECA). Introduction of a methylene group was effective in increasing antiaggregatory potency only when this group is linked to a heteroatom. From these data and those previously reported, the structure-activity relationships derived for the 2-alkynyl-substituted ribose uronamides would indicate that selective potentiation of A2a receptor affinity could be obtained by arom. rings not conjugated with the triple bond or by heteroarom. groups. As for A2a receptors on platelets, the presence of arom. rings, either conjugated or unconjugated to the triple bond, is detrimental for the antiaggregatory activity. Some of the compds. included in this series retain interesting vasodilating properties and merit further investigation for their potential in the treatment of cardiovascular disorders.

IT 141018-26-0

CN

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of aralkynyl and heteroalkynyl derivs. of carboxamidoadenosine as selective A2a adenosine receptor agonists)

RN 141018-26-0 HCAPLUS

.beta.-D-Ribofuranuronic acid, 1-(6-amino-2-iodo-9H-purin-9-y1)-1-deoxy-

2,3-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 162936-24-5P 162936-39-2P 162936-40-5P 162936-41-6P 162936-42-7P 162936-43-8P

162936-44-9P 162936-45-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of aralkynyl and heteroalkynyl derivs. of carboxamidoadenosine as selective A2a adenosine receptor agonists)

RN 162936-24-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-(6-amino-2-iodo-9H-purin-9-yl)-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 162936-39-2 HCAPLUS

CN Benzenepropanoic acid, 4-[[6-amino-9-[N-ethyl-2,3-0-(1-methylethylidene)-.beta.-D-ribofuranuronamidosyl]-9H-purin-2-yl]ethynyl]- (9CI) (CA INDEX NAME)

RN 162936-40-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(5-phenyl-1-pentynyl)-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 162936-41-6 HCAPLUS

CN .beta.-D-Ribofuranuronamide, l-[6-amino-2-[3-(1H-imidazol-1-yl)-1-propynyl]-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

RN 162936-42-7 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-[3-(1-piperidiny1)-1-propyny1]-9H-purin-9-y1]-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 162936-43-8 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-[3-(4-methyl-1-piperazinyl)-1-propynyl]-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 162936-44-9 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-[3-(4-morpholinyl)-1-propynyl]-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

162936-45-0 HCAPLUS RN

.beta.-D-Ribofuranuronamide, 1-[6-amino-2-[3-(4-thiomorpholinyl)-1-CN propynyl]-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

### Absolute stereochemistry.

L29 ANSWER 12 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1995:346678 HCAPLUS

DOCUMENT NUMBER:

122:106395

TITLE:

preparation of adenosine sulfohydrocarbon radicals for

treatment of ischemia or hypoxia in mammals

INVENTOR(S):

Jacobson, Kenneth A.; Maillard, Michel C.

PATENT ASSIGNEE(S):

United States Dept. of Health and Human Services, USA

SOURCE:

PCT Int. Appl., 42 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. APPLICATION NO. DATE KIND DATE -----WO 9402497 19940203 WO 1993-US6590 19930713 A1

W: AU, CA, JP

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9347724 Al 19940214 AU 1993-47724 19930713 US 5498605 A 19960312 US 1994-278704 19940721 PRIORITY APPLN. INFO.: US 1992-914428 A 19920715 WO 1993-US6590 W 19930713

MARPAT 122:106395

OTHER SOURCE(S):

GI

AB The adenosine derivs., e.g. I, wherein at least one of R1-R6 is a sulfohydrocarbon radical, the remaining R groups are non-sulfohydrocarbon radicals, and W is -OCH2-, -NHCH2-, -SCH2-, or -NH(CO)-. Thus, 6-chloropurine riboside reacted with sulfonylamine in BuOH and NEt3 gave N6-p-sulfophenyladenosine. Methods of prepg. such compds., as well as methods of using such compds. to treat ischemia or hypoxia in mammals and pharmaceutical compns. contg. such compds. as the active ingredients, are also described. Binding of I with A1 and A2 adenosine receptors at rat brain is reported.

IT 3250-02-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of adenosine sulfohydrocarbon radicals)

RN 3250-02-0 HCAPLUS

CN Adenosine, 2',3'-O-(ethoxymethylene)- (9CI) (CA INDEX NAME)

L29 ANSWER 13 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1995:261298 HCAPLUS

DOCUMENT NUMBER:

123:228787

TITLE:

Preparation of adenosine analogs as antihypertensives

and antiischemics.

INVENTOR(S):

Spada, Alfred P.; Fink, Cynthia A.; Myers, Michael R.

Rhone-Poulenc Rorer Pharmaceuticals Inc., USA

PATENT ASSIGNEE(S): SOURCE:

U.S., 25 pp. Cont.-in-part of U.S. Ser. No. 587,884,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5364862	A	19941115	US 1992-955783	19921002
CA 2092305	AA	19920326	CA 1991-2092305	19910925
AT 147074	E	19970115	AT 1991-917927	19910925
ES 2095960	Т3	19970301	ES 1991-917927	19910925
SG 80526	A1	20010522	SG 1996-3118	19910925
US 5561134	Α	19961001	US 1994-316761	19941003
US 5736554	Α	19980407	US 1995-455361	19950531
US 5652366	Α	19970729	US 1995-484811	19950607
PRIORITY APPLN. INFO.	:		US 1990-587884 B2	19900925
			US 1992-955783 A2	19921002
			US 1994-229882 B2	19940419
			US 1994-316761 A1	19941003

OTHER SOURCE(S):

MARPAT 123:228787

GI

$$Q^{1=} \xrightarrow{(\mathbb{Z}^{2})_{n}} \mathbb{R}^{b} \qquad \qquad Q^{2=} \xrightarrow{(\mathbb{Z}^{2})_{n}} \mathbb{R}^{a}$$

- AB Title compds. [I; K = N, NO, CH; Q = CH2, O; T = R2, R1R2NCO, R3OCH2; X = alkylene, cycloalkylene, cycloalkenylene; Y = NR4, O, S; a = 0, 1; Z = Q1, Q2; Z1 = N, CR5, (CH)mCR5, (CH)mN; m = 1, 2; Z2 = N, NR6, O, S; n = 0, 1; R1-R6 = H, alkyl, aryl, heterocyclyl; Ra, Rb = H, OH, alkyl, hydroxyalkyl, alkylmercaptyl, thioalkyl, alkoxy, alkoxyalkyl amino, alkylamino, carboxyl, acyl halo, carbamoyl, alkylcarbamoyl, aryl, heterocyclyl; R', R'' = H, alkyl, aralkyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, acyl, alkoxycarbonyl, aralkoxycarbonyl, aryloxycarbonyl; R'R'' = CO, CS, CHORc, CRdRe; Rc, Rd, Re = H, alkyl; RdRe = atoms to form a cycloalkyl ring; with provisos], were prepd. Thus, N6-[trans-2-(thiophen-2-yl)cyclohex-1-yl]adenosine, prepd. from 6-chloropurine riboside and the corresponding amine, at 5 mg/kg orally in rats reduced mean arterial blood pressure and heart rate by 45% and 22%, resp.
- IT 165115-09-3P
  RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
  (prepn. of adenosine analogs as antihypertensives and antiischemics)
  RN 165115-09-3 HCAPLUS
- CN .beta.-D-Ribofuranuronamide, l-deoxy-N-ethyl-2,3-O-(1-methylethylidene)-1[6-[[6-(2-thienyl)-3-cyclohexen-1-yl]amino]-9H-purin-9-yl]- (9CI) (CA
  INDEX NAME)

L29 ANSWER 14 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1994:621999 HCAPLUS

DOCUMENT NUMBER:

121:221999

TITLE:

Preparation of adenosine kinase-inhibiting purine

nucleoside analogs as antiinflammatory agents

INVENTOR(S):

Firestein, Gary Steven; Ugarkar, Bheemarao Ganapatrao; Miller, Leonard Paul; Gruber, Harry Edward; Bullough, David Andrew; Erion, Mark David; Castellino, Angelo

John

PATENT ASSIGNEE(S):

SOURCE:

Gensia, Inc., USA

PCT Int. Appl., 114 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.				KIND DATE													
							WO 1994-US1340						19940203				
	W:	ΑT,	AU,	BB,	BG,	BR,	CA,	CH,	CN	, CZ,	DE,	DK,	ES,	FI,	GB,	ΗU,	JP,
					LU,	MG,	MN,	MW,	NL	, NO,	ΝZ,	PL,	PT,	RO,	RU,	SD,	SE,
		•	UA,														
	RW:							-		, GR,		•				PT,	SE,
		•	•	•		•	•			, ML,		•	•	•			
										AU 19							
EP	6825	19		A.	1	1995	1122		]	EP 19	94-9	0955	8	1994	0203		
		CH,	•	•	•	•											
US																	
PRIORIT	Y APP	LN.	Info	. :				1	JS :	1993-:	1419	0	Α	1993	0203		
								Ţ	JS :	1989-	4087	07	B2	1989	0915		
								Į	JS :	1990-	4669	79	B2	1990	0118		
								Ţ	JS :	1991-	6471	17	B2	1991	0123		
								1	JS :	1991-	8129	16	B2	1991	1223		
								Į	JS :	1994-	1926	45	В1	1994	0203		
								1	NO :	1994-1	JS13	40	W	1994	0203		
OTHER SO	OURCE	(S):			MAR	PAT	121:2	2219	99								

Ι

AΒ Novel nucleosides I [A = O, CH2, S; B' = (CH2)nB, alkenyl, alkynyl; B = H, alkyl, alkoxy, NH2, alkylamino, etc.; C1, C2 = H, acyl, hydrocarbyloxycarbonyl, or C1C2 = C(:O), .alpha.-alkoxyalkylidene; X = CD; D = H, halo, alkyl, cyano, CO2H, etc.; Y = N, CE; E = H, halo, alkyl, alkylthio; F = alkyl, aryl, halo, cyano, indolyl, pyrrolidinyl, etc.; G = H, halo, alkyl, alkoxy, alkylamino, alkylthio; n = 1-4], prepd. by multistep procedures which are described, selectively inhibit adenosine kinase and are useful in treatment of conditions characterized by an inflammatory response. Such conditions include sepsis, arthritis, autoimmune disease, burns, psoriasis, conjunctivitis, etc. Thus, mice with endotoxemia resulting from injection of Escherichia coli lipopolysaccharide showed a dose-dependent increase in survival in response to i.v. injection of the adenosine kinase inhibitor, 4-amino-1-(5-amino-5-deoxy-1-.beta.-D-ribofuranosyl)-3-bromopyrazolo[3,4d]pyrimidine-HCl; this effect was antagonized by the adenosine receptor antagonist 8-(p-sulfophenyl)theophylline.

IT 20789-78-0 21950-36-7

RL: RCT (Reactant); RACT (Reactant or reagent) (prepn. of adenosine kinase-inhibiting purine nucleoside analogs as antiinflammatory agents)

RN 20789-78-0 HCAPLUS

CN Adenosine, 8-bromo-2',3'-O-(1-methylethylidene)-, 5'-(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

RN 21950-36-7 HCAPLUS
CN Adenosine, 5'-amino-5'-deoxy-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 144927-45-7P 158077-68-0P 158077-70-4P 158077-71-5P 158077-74-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of adenosine kinase-inhibiting purine nucleoside analogs as antiinflammatory agents)

RN 144927-45-7 HCAPLUS

CN Adenosine, 8-bromo-N-formyl-2',3'-O-(1-methylethylidene)-, 5'-(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

RN 158077-68-0 HCAPLUS

CN Adenosine, 5',8-diazido-5'-deoxy-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 158077-70-4 HCAPLUS

CN 9H-Purine, 6-(2,3-dihydro-lH-indol-1-yl)-9-[2,3-0-(1-methylethylidene)-.beta.-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

RN 158077-71-5 HCAPLUS

CN 9H-Purine, 6-(2,3-dihydro-1H-indol-1-yl)-9-[2,3-0-(1-methylethylidene)-5-0-[(4-methylphenyl)sulfonyl]-.beta.-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 158077-74-8 HCAPLUS

CN Adenosine, 5',8-diazido-5'-deoxy-N-formyl-2',3'-O-(1-methylethylidene)(9CI) (CA INDEX NAME)

L29 ANSWER 15 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1993:496074 HCAPLUS

DOCUMENT NUMBER:

119:96074

TITLE:

Preparation of adenosine derivatives as cardiovascular

agents.

INVENTOR(S):

Matsuda, Akira; Azebiru, Toichi; Yamaguchi, Toyofumi;

Watanabe, Yoko; Miyashita, Takanori

PATENT ASSIGNEE(S):

Yamasa Shoyu Co., Ltd., Japan Jpn. Kokai Tokkyo Koho, 29 pp.

SOURCE:

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATE	ENT NO.	KIND	DATE		APPLICATION NO.	DATE
JP 0	5025195	<b>A</b> 2	19930202		JP 1991-202598	19910717
JP 3	025559	B2	20000327			•
PRIORITY	APPLN. INFO.:	:	•	JP <sup>,</sup>	1990-191285 ≥RA	1 19900719
				JΡ	1990-218690 A	1 19900820

OTHER SOURCE(S):

MARPAT 119:96074

GI

$$\begin{array}{c|c}
NH2 \\
N \\
N \\
N
\end{array}$$

$$C \equiv C - R^2$$

$$HO OH$$

AB The title compds. [I; R1 = (un)substituted carbamoyl, CO2H,

I

alkoxycarbonyl, CH2-N3, (un) substituted aminomethyl, etc.; R2 = {hydroxy)alkyl}, useful for treatment of brain ischemia, heart ischemia, and hypertension, are prepd. E.g., 2-iodoadenosine was condensed with acetone, the resulting 2',3'-O-isopropylidene deriv. in MeCN-CHCl3 was oxidized with K periodate in H2O, the product was esterified with MeOH, the resulting Me ester was treated with methanolic NH3, the resulting carboxamide was heated with 1-hexyne in DMF contg. Pd(PPh3)2, CuCl, and Et3N, and the resulting 2-(1-hexynyl)-2',3'-isopropylideneadenosine-4'-carboxamide was deprotected to give 2-(1-hexynyl)-adenosine-4'-carboxamide, which had an ED50 of 0.13 .mu.g/Kg in spontaneously hypertensive mice.

IT 142102-95-2P

RN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of, as cardiovascular agent)

142102-95-2 HCAPLUS

CN Adenosine, 5'-deoxy-2-(1-hexynyl)-5'-[[(methylamino)thioxomethyl]amino]-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141018-26-0 HCAPLUS

CN .beta.~D-Ribofuranuronic acid, 1-(6-amino-2-iodo-9H-purin-9-yl)-1-deoxy-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142102-84-9 HCAPLUS

CN .beta.-D-Ribofuranuronic acid, 1-(6-amino-2-iodo-9H-purin-9-yl)-1-deoxy-2,3-O-(1-methylethylidene)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142102-85-0 HCAPLUS

CN .beta.-D-Ribofuranuronic acid, 1-[6-amino-2-(1-hexynyl)-9H-purin-9-yl]-1-deoxy-2,3-O-(1-methylethylidene)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Me 
$$\frac{Me}{N}$$
  $\frac{Me}{N}$   $\frac{N}{N}$   $\frac{C}{N}$   $\frac{C}{N}$ 

RN 142102-86-1 HCAPLUS

CN Adenosine, 2-(1-hexynyl)-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142102-87-2 HCAPLUS

CN Adenosine, 5'-azido-5'-deoxy-2-(1-hexynyl)-2',3'-O-(1-methylethylidene)(9CI) (CA INDEX NAME)

RN 142102-90-7 HCAPLUS

CN Adenosine, 5'-amino-5'-deoxy-2-(1-hexynyl)-2',3'-0-(1-methylethylidene)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142102-91-8 HCAPLUS

CN Adenosine, 5'-deoxy-5'-(formylamino)-2-(1-hexynyl)-2',3'-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

RN 142102-92-9 HCAPLUS

CN Adenosine, 5'-(acetylamino)-5'-deoxy-2-(1-hexynyl)-2',3'-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142102-93-0 HCAPLUS

CN Adenosine, 5'-deoxy-2-(1-hexynyl)-2',3'-0-(1-methylethylidene)-5'[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142102-94-1 HCAPLUS

CN Adenosine, 5'-deoxy-2-(1-hexynyl)-5'-[[(methylamino)carbonyl]amino]-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

RN 142103-01-3 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(1-hexynyl)-9H-purin-9-yl]-1-deoxy-2,3-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Me 
$$M = 0$$
  $M = 0$   $M$ 

RN 142103-03-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(1-hexynyl)-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

RN 142103-04-6 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(1-hexynyl)-9H-purin-9-yl]-N-cyclopropyl-1-deoxy-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 149037-59-2 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-(6-amino-2-iodo-9H-purin-9-yl)-1-deoxy-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 149037-60-5 HCAPLUS

CN .beta.-D-Ribofuranuronic acid, 1-[6-amino-2-(3-hydroxy-1-propynyl)-9H-purin-9-yl]-1-deoxy-2,3-0-(1-methylethylidene)-, methyl ester (9CI) (CA INDEX NAME)

RN 149037-61-6 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(3-hydroxy-1-propyny1)-9H-purin-9-y1]-1-deoxy-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L29 ANSWER 16 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1993:234420 HCAPLUS

DOCUMENT NUMBER:

118:234420

TITLE:

Adenosine kinase inhibitors

INVENTOR(S):

Browne, Clinton E.; Ugarkar, Bheemarao G.; Mullane,

Kevin M.; Gruber, Harry E.; Bullough, David A.; Erion,

Mark D.; Castellino, Angelo

PATENT ASSIGNEE(S):

Gensia Pharmaceuticals, Inc., USA

SOURCE:

Eur. Pat. Appl., 87 pp. CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 496617	A1	19920729	EP 1992-300580	19920123
EP 496617	B1	19991201		
7 . T		D11 D0 DD		140 111 DM

CA	2100863		AA	19920724		CA	1992-210086	63	19920121
WO	9212718		A1	19920806		WO	1992-US515		19920121
	W: AU,	CA, E	ri, No						
AU	665184		B2	19951221		ΑU	1992-13599		19920121
AU	9213599		A1	19920827					
JР	05112595	5	A2	19930507		JР	1992-10094		19920123
IL	100742		A1	19960618		IL	1992-100742	2	19920123
AT	187175		E	19991215		ΑT	1992-300580	)	19920123
ИО	9302628		Α	19930923		NO	1993-2628		19930721
NO	180418		В	19970106					
NO	180418		С	19970416					
บร	5646128		Α	19970708			1994-349125	5	19941201
PRIORITY	APPLN.	INFO.:	:		US	199	1-647117	Α	19910123
					US	199	31-812916	Α	19911223
					US	198	39-408707		19890915
					บร		0-466979		19900118
					MO		2-US515	W	19920121
					US		3-14190		19930203
					บร	199	4-192645	В1	19940203

OTHER SOURCE(S):

MARPAT 118:234420

GI

AB Nucleoside analogs I [A = O, CH2, S; B = (un)substituted C1-4 alkyl; C, C1 = H, protective group(s); X = (un)substituted CH; Y = N, (un)substituted CH; F = alkyl, aryl, aralkyl, halogen, (un)substituted NH2, substituted OH or SH, cyano, cyanoalkyl; G = H, halogen, alkyl, alkoxy, alkylamino, alkylthio] were prepd. Thus, the analog II was prepd. from the pyrimidinone via the azide. II has an adenosine kinase-inhibiting ED50 of <10 nM and was effective in improving post-ischemic functional recovery in isolated guinea pig heart and in preclin. angina models.

IT 21950-36-7

RL: RCT (Reactant); RACT (Reactant or reagent)
 (formylation of)

RN 21950-36-7 HCAPLUS

CN Adenosine, 5'-amino-5'-deoxy-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

$$\begin{array}{c|c}
 & H_2N \\
 & Me \\
 & R \\
 & N \\
 & NH_2 \\
\end{array}$$

IT 144927-50-4P 144927-52-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and deisopropylidenation of)

RN 144927-50-4 HCAPLUS

CN Adenosine, 5'-deoxy-5'-(formylamino)-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 144927-52-6 HCAPLUS

CN 9H-Purine, 9-[2,3-O-(1-methylethylidene)-5-O-[(4-methylphenyl)sulfonyl]-.beta.-D-ribofuranosyl]-6-(octahydro-1H-indol-1-yl)- (9CI) (CA INDEX NAME)

## IT 144927-45-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of, with azide)

RN 144927-45-7 HCAPLUS

CN Adenosine, 8-bromo-N-formyl-2',3'-O-(1-methylethylidene)-, 5'-(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

## IT 144927-51-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and tosylation of)

RN 144927-51-5 HCAPLUS

CN 9H-Purine, 9-[2,3-O-(1-methylethylidene)-.beta.-D-ribofuranosyl]-6-(octahydro-1H-indol-1-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L29 ANSWER 17 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1992:470205 HCAPLUS

DOCUMENT NUMBER:

117:70205

TITLE:

Nucleosides and nucleotides. 112.

2-(1-Hexyn-1-yl)adenosine-5'-uronamides: a new entry

of selective A2 adenosine receptor agonists with

potent antihypertensive activity

AUTHOR(S):

Homma, Hiroshi; Watanabe, Yohko; Abiru, Toichi;

CORPORATE SOURCE:

SOURCE:

Murayama, Toshihiko; Nomura, Yasuharu; Matsuda, Akira Fac. Pharm. Sci., Hokkaido Univ., Sapporo, 060, Japan Journal of Medicinal Chemistry (1992), 35(15), 2881-90

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE:

LANGUAGE:

Journal English

GI

- AΒ Chem. modifications of the potent A2 adenosine receptor agonist 2-(hexynyl)adenosine I (R = R1, R2 = OH) (II) at the 5'-position have been carried out to find more potent and selective A2 agonists. These analogs were evaluated for adenosine A1 and A2 receptor binding affinity in rat brain tissues and antihypertensive effects in spontaneously hypertensive rats (SHR). Among the series of compds., I (R = R3,R4 = cyclopropyl) had the most potent affinity to the A2 receptor with a Ki of 2.6 nM, which is essentially the same as that of the parent agonist II. However, the most selective agonist for the A2 receptor was 2-(1-hexyn-1-yl) adenosine-5'-N-methyluronamide I (R = R3, R4 = Me) with a Ki of 11 nM and a 162-fold selectivity. Therefore, the A1/A2 selectivity was consequently increased. Other 5'-deoxy-5'-substituted derivs., e.g. I [R = R1, R2 = C1 (III); R = R3, R4 = H, Me, NHMe), were also prepd. Amongthese nucleosides, no active compds. with potent or selective affinities to both receptors were found except III. Although glycosyl conformations and sugar-puckering of these nucleosides were studied by 1H NMR spectroscopy, there were no pos. correlations between active and inactive agonists. I (R = R3, R4 = H, cyclopropyl) had a potent hypotensive effect at ED30 values of 0.18 and 0.17 .mu.g/kg, resp., upon i.v. administration to anesthetized SHR.
- IT 142102-85-0P 142102-90-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and amidation of)

RN 142102-85-0 HCAPLUS

CN .beta.-D-Ribofuranuronic acid, 1-[6-amino-2-(1-hexynyl)-9H-purin-9-yl]-1-deoxy-2,3-0-(1-methylethylidene)-, methyl ester (9CI) (CA INDEX NAME)

RN 142102-90-7 HCAPLUS

CN Adenosine, 5'-amino-5'-deoxy-2-(1-hexynyl)-2',3'-O-(1-methylethylidene)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{R} \\ \text{R} \\ \text{R} \\ \text{N} \\ \text{N} \\ \text{NH}_2 \end{array}$$

IT 142102-86-1P

RN 142102-86-1 HCAPLUS

CN Adenosine, 2-(1-hexynyl)-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

IT 142102-84-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and coupling of, with hexyne)

RN 142102-84-9 HCAPLUS

CN .beta.-D-Ribofuranuronic acid, 1-(6-amino-2-iodo-9H-purin-9-y1)-1-deoxy-2,3-O-(1-methylethylidene)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 142102-91-8P 142102-92-9P 142102-93-0P

142102-94-1P 142102-95-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and deblocking of)

RN 142102-91-8 HCAPLUS

CN Adenosine, 5'-deoxy-5'-(formylamino)-2-(1-hexynyl)-2',3'-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

RN

142102-92-9 HCAPLUS Adenosine, 5'-(acetylamino)-5'-deoxy-2-(1-hexyny1)-2',3'-0-(1-CNmethylethylidene) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142102-93-0 HCAPLUS

Adenosine, 5'-deoxy-2-(1-hexynyl)-2',3'-0-(1-methylethylidene)-5'-CN [(methylsulfonyl)amino] - (9CI) (CA INDEX NAME)

RN 142102-94-1 HCAPLUS

CN Adenosine, 5'-deoxy-2-(1-hexynyl)-5'-[[(methylamino)carbonyl]amino]-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142102-95-2 HCAPLUS

CN Adenosine, 5'-deoxy-2-(1-hexynyl)-5'-[[(methylamino)thioxomethyl]amino]-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142103-01-3 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(1-hexynyl)-9H-purin-9-yl]-1-deoxy-2,3-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)

RN 142103-02-4 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(1-hexynyl)-9H-purin-9-yl]-1-deoxy-N-methyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142103-03-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(1-hexynyl)-9H-purin-9-yl]-1-deoxy-N-ethyl-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

RN 142103-04-6 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(1-hexynyl)-9H-purin-9-yl]-N-cyclopropyl-1-deoxy-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142103-05-7 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(1-hexynyl)-9H-purin-9-yl]-1-deoxy-2,3-0-(1-methylethylidene)-N-propyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 142103-06-8 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-amino-2-(1-hexynyl)-9H-purin-9-yl]-N-butyl-1-deoxy-2,3-0-(1-methylethylidene)- (9CI) (CA INDEX NAME)



## IT 141018-26-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
 (prepn. and esterification of)

RN 141018-26-0 HCAPLUS

CN .beta.-D-Ribofuranuronic acid, 1-(6-amino-2-iodo-9H-purin-9-yl)-1-deoxy-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

## IT 142102-87-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
 (prepn., chlorination, and redn. of)

RN 142102-87-2 HCAPLUS

CN Adenosine, 5'-azido-5'-deoxy-2-(1-hexynyl)-2',3'-O-(1-methylethylidene)-(9CI) (CA INDEX NAME)

IT 141018-25-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn., oxidn., and coupling of, with hexyne)

RN 141018-25-9 HCAPLUS

CN Adenosine, 2-iodo-2',3'-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L29 ANSWER 18 OF 39 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1992:236101 HCAPLUS

DOCUMENT NUMBER:

116:236101 HC

TITLE:

Preparation of new adenosine derivatives as

cardiovascular agents.

INVENTOR(S):

Gadient, Fulvio

PATENT ASSIGNEE(S):

Sandoz-Patent-G.m.b.H., Germany

SOURCE:

Ger. Offen., 8 pp. CODEN: GWXXBX

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

1

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DE 4025879	A1	19920220	DE 1990-4025879	19900816

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CA 2064869
                       AΑ
                            19920217
                                            CA 1991-2064869
                                                             19910813
     WO 9203463
                       A1
                            19920305
                                            WO 1991-CH170
         W: AU, CA, CS, FI, HU, JP, KR, PL, SU, US
                                                             19910813
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
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         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
     HU 60504
                       A2
                            19920928
                                           HU 1992-1080
                                                             19910813
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                       T2
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                                           ZA 1991-9267
                                                             19911212
     RO 110236
                       B1
                            19951130
                                           RO 1992-152
                                                            19920213
PRIORITY APPLN. INFO.:
                                        DE 1990-4025879 A 19900816
                                        WO 1991-CH170
                                                         A 19910813
OTHER SOURCE(S):
                        MARPAT 116:236101
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The title compds. [I; R1 = H, alkyl, cycloalkyl, Ph, (substituted) AΒ phenylalkyl; R2 = H, alkyl, halo, cycloalkyl; R3 = CH2OH, CONHR4; R4 = H, alkyl, cycloalkyl; X = 0, S], useful for the treatment of hypertension, thrombolism, supraventricular tachycardia, etc. (no data), were prepd. Cyclocondensation of 1'-deoxy-1'-(6-p-methoxyanilino-2methyl-9-purinyl)-.beta.-D-ribofuranuronic acid N-ethylamide with 1.1'-carbonyldi-1H-imidazole in DMF at room temp. for 5 h gave I [R1 = p-MeOC6H4, R2 = Me, R3 = EtNHCO, X = O. ΙT 141426-21-3P 141426-22-4P 141426-23-5P 141426-24-6P 141426-25-7P 141426-26-8P 141426-27-9P 141426-28-0P 141426-29-1P 141426-30-4P 141426-31-5P 141426-32-6P 141426-33-7P 141426-34-8P 141426-35-9P 141426-36-0P 141426-37-1P 141426-38-2P 141426-39-3P 141426-40-6P 141426-41-7P 141426-42-8P 141426-43-9P 141448-37-5P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of, as cardiovascular agent)

RN 141426-21-3 HCAPLUS

.beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-[(4-methoxyphenyl)amino]-2-methyl-9H-purin-9-yl]-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141426-22-4 HCAPLUS

CN Adenosine, N-cyclohexyl-, cyclic 2',3'-carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141426-23-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-(cyclopentylamino)-2-methyl-9H-purin-9-yl]-1-deoxy-N-ethyl-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

RN 141426-24-6 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-(cyclopentylamino)-9H-purin-9-yl]-1-deoxy-N-ethyl-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141426-25-7 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-(cyclohexylamino)-9H-purin-9-yl]-1-deoxy-N-ethyl-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

RN 141426-26-8 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-[(4-methoxyphenyl)amino]-9H-purin-9-yl]-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141426-27-9 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-(phenylamino)-9H-purin-9-yl]-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

RN 141426-28-0 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-[(4-fluorophenyl)amino]-9H-purin-9-yl]-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141426-29-1 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-[(4-chlorophenyl)amino]-9H-purin-9-yl]-1-deoxy-N-ethyl-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

RN 141426-30-4 HCAPLUS

.beta.-D-Ribofuranuronamide, 1-[6-(cyclohexylamino)-2-methyl-9H-purin-9-yl]-1-deoxy-N-ethyl-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141426-31-5 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[2-methyl-6-[(1-methylethyl)amino]-9H-purin-9-yl]-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

RN 141426-32-6 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[2-methyl-6-(phenylamino)-9H-purin-9-yl]-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141426-33-7 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-[(4-fluorophenyl)amino]-2-methyl-9H-purin-9-yl]-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

RN 141426-34-8 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-[(4-chlorophenyl)amino]-2-methyl-9H-purin-9-yl]-1-deoxy-N-ethyl-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141426-35-9 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-[(4-methoxyphenyl)amino]-2-methyl-9H-purin-9-yl]~, cyclic 2,3-carbonothioate (9CI) (CA INDEX NAME)

RN 141426-36-0 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-(6-amino-2-methyl-9H-purin-9-yl)-1-deoxy-N-ethyl-, cyclic 2,3-carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141426-37-1 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-[(4-methoxyphenyl)amino]-9H-purin-9-yl]-, cyclic 2,3-carbonothioate (9CI) (CA INDEX NAME)

RN 141426-38-2 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-[6-[(4-chlorophenyl)amino]-2-methyl-9H-purin-9-yl]-1-deoxy-N-ethyl-, cyclic 2,3-carbonothioate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141426-39-3 HCAPLUS

CN .beta.-D-Ribofuranuronamide, 1-deoxy-N-ethyl-1-[6-[(4-fluorophenyl)amino]-2-methyl-9H-purin-9-yl]-, cyclic 2,3-carbonothioate (9CI) (CA INDEX NAME)

RN 141426-40-6 HCAPLUS

CN Adenosine, N-(4-methoxyphenyl)-, cyclic 2',3'-carbonate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141426-41-7 HCAPLUS

CN Adenosine, N-(4-chlorophenyl)-, cyclic 2',3'-carbonate (9CI) (CA INDEX NAME)